

AMENDMENTS TO THE CLAIMS

Listing of Claims

This Listing of Claims will replace all prior versions and listings of claims in the application.

1-19 (Canceled).

20. (Currently amended) The composition according to claim ~~[[19]]~~ 46, further comprising an additional agent selected from an immunosuppressant, an anti-cancer agent, an anti-viral agent, an anti-inflammatory agent, an antifungal agent, an antibiotic, or an anti-vascular hyperproliferation compound.

21. (Withdrawn-currently amended) A method of treating or preventing an IMPDH-mediated disease or condition in a mammal comprising the step of administering to said mammal a composition according to ~~claim 19 or 20~~ any one of claims 20, 46, 50, and 51.

22. (Withdrawn) The method according to claim 21, wherein said IMPDH-mediated disease or condition is selected from transplant rejection, graft versus host disease, or an autoimmune disease.

23. (Withdrawn) The method according to claim 22, wherein said mammal is administered an additional immunosuppressant in a separate dosage form or as part of said composition.

24. (Withdrawn-currently amended) A method for inhibiting replication of a virus in a mammal comprising the step of administering to said mammal a composition according to ~~claim~~

~~19 or 20~~ any one of claims 20, 46, 50, and 51.

25. (Withdrawn) The method according to claim 24, wherein said virus is selected from orthomyxovirus, paramyxovirus, herpesvirus, retrovirus, flavivirus, pestivirus, hepatotropic virus, bunyavirus, Hantaan virus, Caraparu virus, human papilloma virus, encephalitis virus, arena virus, reovirus, vesicular stomatitis virus, rhinovirus, enterovirus, Lassa fever virus, togavirus, poxvirus, adenovirus, rubiola, or rubella.

26. (Withdrawn) The method according to claim 25, wherein said mammal is administered an additional anti-viral agent in a separate dosage form or as part of said composition.

27. (Withdrawn-currently amended) A method for inhibiting vascular cellular hyperproliferation in a mammal comprising the step of administering to said mammal a composition according to ~~claim 19 or 20~~ any one of claims 20, 46, 50, and 51.

28. (Withdrawn) The method according to claim 27, wherein said method is useful in treating or preventing restenosis, stenosis, arteriosclerosis or other hyperproliferative vascular disease.

29. (Withdrawn) The method according to claim 28, wherein said mammal is administered an additional anti-vascular hyperproliferative agent in a separate dosage form or as part of said composition.

30. (Withdrawn-currently amended) A method for inhibiting tumors and cancer in a mammal comprising the step of administering to said mammal a composition according to ~~claim 19~~

~~or 20~~ any one of claims 20, 46, 50, and 51.

31. (Withdrawn) The method according to claim 30, wherein said medicament is useful to treat or prevent lymphoma, leukemia and other forms of cancer.

32. (Withdrawn) The method according to claim 31, wherein said mammal is administered an additional anti-tumor or anti-cancer agent in a separate dosage form or as part of said composition.

33. (Withdrawn-currently amended) A method for inhibiting inflammation or an inflammatory disease in a mammal comprising the step of administering to said mammal a composition according to ~~claim 19 or 20~~ any one of claims 20, 46, 50, and 51.

34. (Withdrawn) The method according to claim 33, wherein said method is useful for treating or preventing osteoarthritis, acute pancreatitis, chronic pancreatitis, asthma or adult respiratory distress syndrome.

35. (Withdrawn) The method according to claim 33, wherein said mammal is administered an additional anti-inflammatory agent in a separate dosage form or as part of said composition.

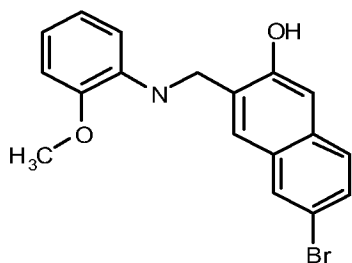
36. (Withdrawn-currently amended) The composition of claim ~~[[19]]~~ 46 or 20, wherein X is -N(R₆)-C(O)-Y-.

37. (Withdrawn) The composition of claim 36, wherein Y is -C(R₁₂)=C(R₁₂)-.

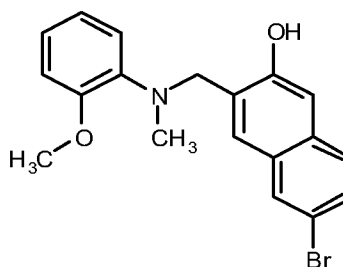
38. (Withdrawn-currently amended) The composition of claim ~~[[19]]~~ 46 or 20,

wherein Q is -N(H)-C(O)-O-.

39. (Withdrawn) A compound selected from the group consisting of 115 and 151;



115



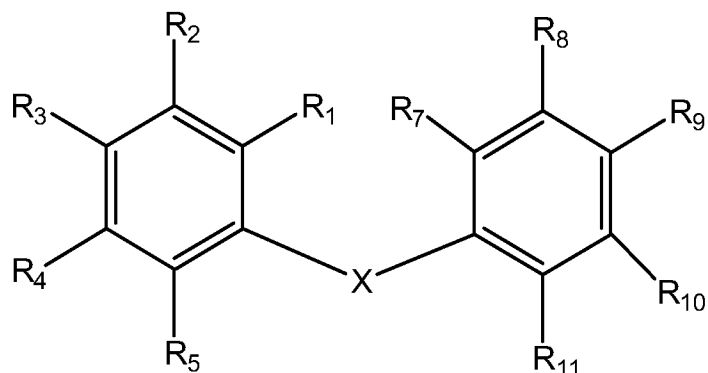
151.

40. (Withdrawn) A compound selected from the group consisting of 101, 103, 104, 105, 106, 107, 110, 111, 112, 113, 114, 116, 117, 118, 119, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 148, 149, 153, 154, 155, 156, 159, 160, 162, 163, 164, 165, 166, 168, 169, 172, 173, 175, 177, 178, 179, 181, 182, 183, 184, 185, 188, 191, 192, 193 and 304.

41-45. (Canceled).

46. (Currently amended) A composition comprising:

a) a compound of the formula:



wherein:

X is selected from -C(O)-N(R₆)-, -N(R₆)-C(O)-, -CH₂-N(R₆)-, -N(R₆)-CH₂-,
 -N(R₆)-S(O)₂-, -S(O)₂-N(R₆)-, -C(R₁₂)(R₁₂)-C(O)-, -C(O)-C(R₁₂)(R₁₂)-, -C(R₁₂)(R₁₂)-S(O)₂-,
 -S(O)₂-C(R₁₂)(R₁₂)-, -S(O)₂-O-, -O-S(O)₂-, -N(R₆)-C(O)-Y- or -Y-C(O)-N(R₆)-; wherein

each R₆ is independently selected from hydrogen, C₁-C₄ straight or branched alkyl,
 C₂-C₄ straight or branched alkenyl or alkynyl, Ar-substituted-C₁-C₄ straight or branched alkyl, or
 Ar-substituted-C₂-C₄ straight or branched alkenyl or alkynyl; wherein

each R₆, except hydrogen, is optionally substituted with up to 3 substituents
 independently selected from halo, hydroxy, nitro, cyano or amino;

each R₁₂ is independently selected from R₆, W-[C₁-C₄ straight or branched alkyl],
 W-[C₂-C₄ straight or branched alkenyl or alkynyl], Ar-substituted-[W-[C₁-C₄ straight or branched
 alkyl]], Ar-substituted-[W-[C₂-C₄ straight or branched alkenyl or alkynyl]], O-Ar, N(R₆)-Ar, S-Ar,
 S(O)-Ar, S(O)₂-Ar, S-C(O)H, N(R₆)-C(O)H, or O-C(O)H; wherein

W is O-, O-C(O)-, S-, S(O)-, S(O)₂-, S-C(O)-, N(R₆)-, or N(R₆)-C(O)-; and wherein

each R₁₂ is optionally and independently substituted with up to 3 substituents independently selected from halo, hydroxy, nitro, cyano or amino;

Y is selected from -O-, -S-, -C≡C-, -C(R₁₂)₂-C(R₁₂)₂-, -C(R₁₂)₂- or -C(R₁₂)=C(R₁₂)-;

each of R₁, R₂, R₃, R₄, R₅, R₇, R₈, R₉, R₁₀, and R₁₁ is independently selected from hydrogen, halo, hydroxy, cyano, nitro, amino, -C(O)NH₂, Z-[(C₁-C₄)-straight or branched alkyl], Z-[(C₂-C₄)-straight or branched alkenyl or alkynyl], Ar-substituted-[(C₁-C₄)-straight or branched alkyl], Ar-substituted-[(C₂-C₄)-straight or branched alkenyl or alkynyl], Ar, Q-Ar, [(C₁-C₄)-straight or branched alkyl]-Q-Ar, [(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-Ar, O-[(C₁-C₄)-straight or branched alkyl]-Q-Ar, O-[(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-Ar, [(C₁-C₄)-straight or branched alkyl]-Q-R₁₃, or [(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-R₁₃, ~~or any two adjacent groups selected from either R₁ and R₂ or R₇, R₈, R₉, R₁₀, and R₁₁ may be taken together with the carbon atoms to which they are bound to form a 5 to 6-membered aromatic carbocyclic or heterocyclic ring;~~ and

~~R₃ and R₄ are taken together with the carbon atoms to which they are bound to form a 5 to 6-membered aromatic carbocyclic or heterocyclic ring;~~

wherein two adjacent groups selected from either R₁, R₂, R₃, R₄, and R₅ or R₇, R₈, R₉, R₁₀, and R₁₁, are taken together with the carbon atoms to which they are bound to form a 5 to 6 membered aromatic carbocyclic ring or heterocyclic ring; and wherein

Z is selected from a bond, O-, S-, S(O)₂-, C(O)-, OC(O)-, or N(H)C(O)-;

Q is selected from O, -O-C(O)-, -C(O)-O-, -N(H)-C(O)-O-, -O-N(H)-C(O)-, -N(H)-C(O)-, -C(O)-N(H)-, -O-C(O)-N(H)-, or -C(O)-N(H)-O-;

Ar is selected from phenyl, 1-naphthyl, 2-naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, 2-pyrazolynyl, pyrazolidinyl, isoxazolyl, isotriazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, indolizynyl, indolyl, isoindolyl, 3H-indolyl, indolinyl, benzo[b]furanyl, benzo[b]thiophenyl, 1H-indazolyl, benzimidazolyl, benzthiazolyl, purinyl, 4H-quinolizynyl, quinolynyl, isoquinolynyl, 1,2,3,4-tetrahydro-isoquinolynyl, cinnolynyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, piperidinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl or phenoxazinyl or other chemically feasible monocyclic, bicyclic or tricyclic ring systems, wherein each ring consists of 5 to 7 ring atoms and wherein each ring comprises 0 to 3 heteroatoms independently selected from N, O and S;

R₁₃ is selected from [C₁-C₁₂ straight or branched alkyl] or, [C₂-C₁₂ straight or branched alkenyl or alkynyl]; wherein R₁₃ is optionally substituted with 1 to 4 substituents independently selected from R₁₄ or R₁₅, wherein

each R₁₄ is a monocyclic or a bicyclic ring system consisting of 3 to 7 members per ring, wherein said ring system optionally comprises up to 4 heteroatoms selected from N, O, and S; wherein a CH₂ adjacent to said N, O or S may be substituted with C(O); and wherein R₁₄ optionally

comprises up to 2 substituents independently selected from (C₁-C₄)-straight or branched alkyl, (C₂-C₄)-straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, (CH₂)_n-R₁₆, -S-(CH₂)_n-R₁₆, -S(O)-(CH₂)_n-R₁₆, -S(O)₂-(CH₂)_n-R₁₆, -O-(CH₂)_n-R₁₆, or -N(R₁₈)-(CH₂)_n-R₁₆

wherein n is 0, 1 or 2;

R₁₆ is selected from halogen, -CN, -NO₂, -CF₃, -OCF₃, -OH, -S-(C₁-C₄)-alkyl, -S(O)-(C₁-C₄)-alkyl, -S(O)₂-(C₁-C₄)-alkyl, -NH₂, -NH-(C₁-C₄)-alkyl, -N((C₁-C₄)-alkyl)₂, COOH, C(O)-O-(C₁-C₄)-alkyl or O-(C₁-C₄)-alkyl; and

each R₁₅ is independently selected from -OR₁₇, or -N(R₁₈)₂;

R₁₇ is selected from hydrogen, -(C₁-C₆)-straight alkyl, -(C₁-C₆)-straight alkyl-Ar, -C(O)-(C₁-C₆)-straight or branched alkyl, -C(O)-Ar, or -(C₁-C₆)-straight alkyl-CN; and

each R₁₈ is independently selected from -(C₁-C₆)-straight or branched alkyl, -(C₁-C₆)-straight or branched alkyl-Ar, -(C₁-C₆)-straight alkyl-CN, -(C₁-C₆)-straight alkyl-OH, -(C₁-C₆)-straight alkyl-OR₁₇, -C(O)-(C₁-C₆)-straight or branched alkyl, -C(O)-Ar, -S(O)₂-(C₁-C₆)-straight or branched alkyl, or -S(O)₂-Ar; wherein

any alkyl, alkenyl or alkynyl group is optionally substituted with 1 to 3 independently selected halo groups; and

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally substituted with 1 to 3 substituents independently selected from halo, hydroxy, nitro, cyano, amino, (C₁-C₄)-straight or branched alkyl, O-(C₁-C₄)-straight or branched alkyl, (C₂-C₄)-straight or branched alkenyl or

alkynyl, or O-(C₂-C₄)-straight or branched alkenyl or alkynyl;

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally benzofused; with the provisos that:

at least two of R₁, R₂, R₃, R₄, or R₅ is hydrogen;

no more than two of R₁, R₂, R₃, R₄, or R₅ comprises Ar;

at least two of R₇, R₈, R₉, R₁₀ or R₁₁ is hydrogen; and

no more than two of R₇, R₈, R₉, R₁₀ or R₁₁ comprises Ar; and

when X is -C(O)-NH- or -NH-C(O)-, any two adjacent groups selected from R₁, R₂, R₃, R₄, and R₅ are taken together with the carbon atoms to which they are bound to form an unsubstituted fused benzene ring, the remaining three of R₁, R₂, R₃, R₄, and R₅ are one hydroxy group and two hydrogen groups, and four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, then the remaining one of R₇, R₈, R₉, R₁₀, and R₁₁ is not 2-(4-chloro-phenyl)-ethyl, 2-(3,4-dichloro-phenyl)ethyl, 2-(3,4-dimethoxy-phenyl)ethyl, or 2-(1,1'-biphenyl-4-yl)ethyl; and

when X is -C(O)-NH- or -NH-C(O)-, any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are taken together with the carbon atoms to which they are bound to form an unsubstituted fused benzene ring, the remaining three of R₇, R₈, R₉, R₁₀, and R₁₁ are one hydroxy group and two hydrogen groups, and four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, then the remaining one of R₁, R₂, R₃, R₄, and R₅ is not 2-(4-chlorophenyl)-ethyl, 2-(3,4-dichlorophenyl)ethyl, 2-(3,4-dimethoxy-phenyl)ethyl, or 2-(1,1'-biphenyl-4-yl)ethyl;

when X is -SO₂-NH- or -NH-SO₂-, one of R₁, R₂, R₃, R₄, and R₅ is -NH₂, the remaining four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, and any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are taken together with the carbon atoms to which they are bound to form an unsubstituted pyridine ring fused to a benzene ring, then at least one of the remaining R₇, R₈, R₉, R₁₀, and R₁₁ is not hydrogen or -OCH₃;

when X is -SO₂-NH- or -NH-SO₂-, one of R₇, R₈, R₉, R₁₀, and R₁₁ is -NH₂, the remaining four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, and any two adjacent groups selected from R₁, R₂, R₃, R₄, and R₅ are taken together with the carbon atoms to which they are bound to form an unsubstituted pyridine ring fused to a benzene ring, then at least one of the remaining R₁, R₂, R₃, R₄, and R₅ is not hydrogen or -OCH₃;

when X is -SO₂-NH- or -NH-SO₂- and four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, then any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are not taken together with the carbon atoms to which they are bound to form an unsubstituted indole ring, an indole ring substituted by -Cl, =O, -cyano, -CH₃, or -C(O)-CH₃, or an unsubstituted indazole ring; and

when X is -SO₂-NH- or -NH-SO₂- and four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, then any two adjacent groups selected from R₁, R₂, R₃, R₄, and R₅ are not taken together with the carbon atoms to which they are bound to form an unsubstituted indole ring, an indole ring substituted by -Cl, =O, -cyano, -CH₃, or -C(O)-CH₃, or an unsubstituted indazole ring; and

b) a carrier, adjuvant or vehicle, which is pharmaceutically acceptable for oral administration or administration by injection.

47. (Canceled).

48. (Currently amended) The composition according to ~~any one of claims 19-20, 41-42, and 45-46~~ claim 46 or 20, wherein X is -N(H)-C(O)- or -C(O)-N(H)-.

49. (Canceled).

50. (New) A composition comprising:

a) a compound selected from the group consisting of 100, 101, 102, 103, 104, 105, 106, 107, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 148, 149, 151, 152, 153, 154, 155, 156, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 175, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 190, 191, 192, 193, 196, 200, 204, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, and 326; and

b) a carrier, adjuvant, or vehicle, which is pharmaceutically acceptable for oral administration or administration by injection.

51. (New) The composition according to claim 50, further comprising an additional agent selected from an immunosuppressant, an anti-cancer agent, an anti-viral agent, an anti-inflammatory agent, an antifungal agent, an antibiotic, or an anti-vascular hyperproliferation compound.